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## Maturation of oral feeding skills in preterm infants

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### Abstract

**Aim**—Safe and successful oral feeding requires proper maturation of sucking, swallowing and respiration. We hypothesized that oral feeding difficulties result from different temporal development of the musculatures implicated in these functions.

**Methods**—Sixteen medically stable preterm infants (26 to 29 weeks gestation, GA) were recruited. Specific feeding skills were monitored as indirect markers for the maturational process of oral feeding musculatures: rate of milk intake (mL/min); percent milk leakage (lip seal); sucking stage, rate (#/s) and suction/expression ratio; suction amplitude (mmHg), rate and slope (mmHg/s); sucking/swallowing ratio; percent occurrence of swallows at specific phases of respiration. Coefficients of variation (COV) were used as indices of functional stability. Infants, born at 26/27- and 28/29-week GA, were at similar postmenstrual ages (PMA) when taking 1–2 and 6–8 oral feedings per day.

**Results**—Over time, feeding efficiency and several skills improved, some decreased and others remained unchanged. Differences in COVs between the two GA groups demonstrated that, despite similar oral feeding outcomes, maturation levels of certain skills differed.

**Conclusions**—Components of sucking, swallowing, respiration and their coordinated activity matured at different times and rates. Differences in functional stability of particular outcomes confirm that maturation levels depend on infants' gestational rather than PMA.

### Keywords

Bottle feeding; Prematurity; Sucking skills; Suck-swallow-respiration; Swallowing skills; Very low birth weight

## INTRODUCTION

The difficulties that preterm infants have transitioning from tube to independent oral feeding lead to delayed hospital discharge, maternal stress and rising financial burden (1,2). Caretakers recognize that immature sucking, delayed swallow and/or uncoordinated suck, swallow and respiration are potential causes for oral feeding issues (3,4). Within each of these three functions, there are components that may mature at different times as we have shown in the development of the suction and expression components of sucking (5). Thus, it is, conceivable that the difficulty encountered by preterm infants to feed orally results from similar sequential maturation of sucking, swallowing, respiration and/or their coordination.

This study evaluated the level and rate of maturation of components within each of these functions as preterm infants advanced in their oral feeding. Our working premise was that

proper functioning of sucking, swallowing and respiration occurs at two levels; first on the appropriate functional maturation and synchronization of the muscles implicated within each function and, second on the safe coordination between the musculatures of these different functions. Studies have demonstrated that individual and coordinated activities necessitate close interactions between different sets of muscles or musculatures. For instance, in the synchronization of sucking musculature, there is a close correlation between muscles from the perioral area for the generation of sucking pressure, the jaw for its opening and closing and tongue for bolus formation and its peristaltic transport to the pharynx (6,7). The oropharyngeal swallow similarly implicates the participation of a number of pharyngeal musculatures controlling anatomical structures; dysphagia ensuing when compromises in any of these constituents occur (8,9). During oral feeding, the mechanical generation of respiration involves the proper activation of the diaphragmatic, intercostal musculatures, as well as upper airway muscles from nose to glottis (10). To study these individual rhythmic activities, the existence of central pattern generators (CPGs) has been advanced (11–13). CPGs for sucking, swallowing, and respiration have been described anatomically in the medulla with distinct pools of motor neurons involved in the sequential and rhythmic movements of the individual functions (11,12,14). The regulatory feedback of CPGs is presumed to require intact sensory afferents signalling changes in environmental as well as physiologic conditions (15). In addition, in preterm infants, exchange of oxygen/carbon dioxide is not only threatened by the mechanical activity of the respiratory musculature, but also by their immature pulmonary function resulting from dysfunctional alveoli and higher alveolar recoil (16).

Safety in infant oral feeding implies minimal risk of aspiration and requires the adequate coordination of sucking, swallowing and respiration as the anatomical pathways for air and nutrients share the same pharyngeal tract. In addition to their individual rhythmic functionality, these three functions need to occur sequentially from the oral to pharyngeal to pulmonary phases (17). Moreover, swallow needs to occur during a safe phase of the respiratory cycle. Therefore, to assist in our understanding of the coordination of these three functions, it becomes advantageous to incorporate the concept of cross-systems interactions proposed by McFarland and Tremblay (18) with that of CPGs. These studies support our working premise that mechanical maturation of oral feeding skills need to occur at the peripheral and central levels, i.e. muscles and central nervous system.

As these maturational processes cannot be measured directly, we monitored changes over time of specific oral feeding skills that reflected their performance when preterm infants transitioned from tube to oral feeding. We hypothesized that developmental processes of suck, swallow and respiration would be, first, reflected by maturation indices of specific oral feeding skills at different times and/or rates and, second, dependent upon gestational and postmenstrual ages (PMA).

## METHODS

### Subjects

Sixteen infants (8 males, 8 females), born between 26 and 29 weeks gestation ( $27.5 \pm 1.1$ , mean  $\pm$  SD) with birth weights averaging  $1049 \pm 224$ g, were recruited from the nurseries at Texas Children's Hospital, Houston TX, USA. They were appropriate for gestational age (GA) as determined by maternal dates and antenatal ultrasonography. Exclusion criteria included intraventricular haemorrhage grades III and IV, periventricular leukomalacia, necrotizing enterocolitis, hydrocephalus, bronchopulmonary dysplasia and major congenital anomalies. These subjects were clinically stable, i.e. their hospital discharge being primarily dependent upon their ability to attain independent oral feeding. Introduction and advancement of oral feeding was left to the discretion of attending physicians based on an appropriate daily weight

gain of  $\geq 15$  g/kg/day. The study received approval from the Baylor College of Medicine Institutional Review Board for Human Research. Informed consent was obtained from parents.

### Study design/methodology

Oral feeding performance was monitored longitudinally when subjects were taking 1–2 and 6–8 oral feedings/day. To ensure that we did not interfere with breastfeeding, assessments were made when mothers were absent. Infants were offered the milk or formula they were receiving during this period. The oral-motor assessment used a nipple/bottle apparatus previously described (19). Briefly, the suction (S) and expression (E) components of sucking (Sk) were monitored via two catheters placed on the bottle nipple and connected to pressure transducers. Caretakers chose the nipple, at the time of the feeding, they deemed most appropriate for their patient and were asked to let infants feed at their own pace, i.e. with no ‘encouragement’ when they paused/rested. Milk level from a reservoir connected to the nipple chamber was continually adjusted to the level of the infant’s mouth to allow for a self-paced flow, i.e. milk only flows if the infant was sucking (19). Insofar as the nipple chamber was always filled, the subjects could obtain milk whether they used suction and/or expression only (20). Such setup is important as it was a true replication of normal bottle-feeding. Onset of pharyngeal swallowing (Sw) was measured with a small pressure drum held snugly over the infant’s hyoid bone by a soft elastic strap attached to a stockinette cap. Elevation of the hyoid and laryngeal structures is commonly used to identify the start of the pharyngeal swallow (21). Respiratory effort (R) was monitored using another pressure drum taped below the chest over the diaphragm. This measure pertains to changes in lung inflation measured by chest and abdominal movements, but does not allow for quantitative measures such as tidal volume or minute ventilation (22). This approach was selected for the following reasons: 1. to minimize invasiveness as preterm infants often show hypersensitivity of the facial area due to frequent aversive, but necessary, oral and/or nasal procedures; 2. to rely on nasal airflow would not be accurate as many subjects were receiving oxygen via a nasal cannula; 3. to monitor intercostal respiration would not be informative as preterm infants are primarily diaphragmatic breather due to immature intercostals muscles.

### Oral feeding outcomes

Monitored outcomes and their corresponding functional significance are summarized in Table S1 and Figure 1. Within our context, ‘synchronization’ pertains to the interactions of muscles *within* the same musculature and ‘coordination’, that of muscles *between* different musculatures. *Oral feeding efficiency* was measured by the rate of milk intake (total volume transferred minus volume lost during a feeding; mL/min). The duration of a feeding included the ‘out’ times during which the infant needed to burp, cough, and/or rest. These decisions were left to caretakers’ discretion who assessed infants’ need. In our opinion, this provided a more accurate measure of the *actual* performance of the infant. *Maturation of the perioral musculature* implicated in the infant’s ability to latch onto the nipple tightly (lip seal) was evaluated by the percent milk leakage/loss (g) measured by weighing a bib before and after each feeding ( $1\text{ g} \cong 1\text{ mL}$ ) over the total volume taken. *Maturation of sucking* was monitored via Sk rate and stage, suction/expression ratio (S/E) and the time interval between peak suction and expression (S-E, s). Sk rate (number/s) was calculated based on the Sk component *most frequently used*, i.e. S or E, as infants commonly revert to the use of E only. This was used to evaluate the synchrony of the sucking muscles and the rhythmicity of S and/or E. Sk stage was defined by the presence of S and/or E and their rhythmicity. This was rated on a scale of 1 (immature) to 5 (mature) (5). S/E ratio was utilized as an index of the coordination between S and E musculatures with a 1:1 ratio corresponding to the full-term mature stage 5, i.e. rhythmic alternation of S/E (23). Time interval between peak amplitude of S and E (S-E, s) was indicative of the response time between peak activation of these respective musculatures or their coordination. *Maturation of suction musculature* was evaluated in terms of S rate (#S/s),

amplitude (mm Hg) and first derivative (slope, mm Hg/s). S rate was indicative of the synchrony of the S muscles and their rhythmicity for the rhythmic generation of the S component. S amplitude corresponded to the force generated by the S musculature. S slope was used as a reflection of the degree of synchronization of the muscles implicated in generating S; the greater the value, the faster their activation speed. Time interval between start to peak S ( $t_1, s$ ) and between peak to end S ( $t_2, s$ ) was indicative of the duration of the activation and relaxation of the S musculature, respectively. *Maturation of swallow* was evaluated by its rate (#Sw/s) used as an indirect marker of the synchrony of the Sw muscles and their rhythmicity. *Maturation of suck-swallow* was assessed via Sk-Sw ratio and the time intervals between peak S to onset of Sw (S-Sw, s) and peak E to onset of Sw (E-Sw, s). As it is unclear whether E occurs before S or vice versa, onsets of Sw chosen for these measures were those that were closest, be them preceding or following the peak E analyzed. The time interval E-Sw was assigned a negative time value when Sw preceded E and a positive one when following E. This was taken into consideration in the weighted averaging method used in our data analyses (see below). The time interval between peak E and onset of Sw was also necessary when infants only used the E component; this being the predominant pattern when they were introduced to oral feeding. These outcomes were used as markers for the coordination between Sk and Sw musculatures and the response time between end of Sk and activation of the Sw musculature.

To compare the functional stability of the implicated musculatures demonstrated by each gestational group of infants (26–27 vs. 28–29 weeks GA), the coefficients of variation (COV, SD/mean) of S amplitude and time intervals  $t_1$ ,  $t_2$ , S-E, S-Sw, E-Sw were computed when both groups of infants were introduced (1–2 oral feedings/day) and attained independent oral feeding (6–8 oral feedings/day). We define functional stability as subjects' variability in executing particular skills, e.g. the smaller the COV, the more infants have attained similar levels of ability for those skills. This measure indirectly provides information on their different time(s) and rate(s) of maturation.

Safe Sw-R coordination was assessed as the percent occurrence of Sw at specific phases of R (Sw-R interfacings; Fig. 2). Swallows may occur at the start of inspiration/end exhalation (start I); during inhalation (i); at end inspiration/start exhalation (end I); during exhalation (e); while interrupting inhalation (ii) and/or exhalation (ie); and/or during deglutition apnea (DA), the latter being characterized by an apneic episode  $\geq 2$  sec (23). We speculated that mature coordination of Sw and R would be represented by a shift from 'unsafe' to 'safer' Sw-R interfacings. Unsafe Sw-R interfacings were defined as those during which swallowing occurred during DA and inhalation as risks of oxygen desaturation and aspiration, respectively, would be highest.

## Data analyses

Sucking, swallowing and respiratory variables were computed using a weighted averaging approach. Each oral feeding session was divided into three equal time periods to take into account potential changes in performance over the duration of the feedings that may be due to factors such as fatigue; the latter more likely to occur in the last period. This approach was based on the fact that each measure was weighted to reflect their relative importance over the entire feeding session. The average sucking burst duration per time period was computed from all the sucking bursts within each period. The sucking burst closest in duration to that computed average *with* the most representative sucking pattern was selected for subsequent analyses. A weighted average for each variable was computed based on the following equation:  $[T_1(B_1) + T_2(B_2) + T_3(B_3)] / (T_1 + T_2 + T_3)$ .  $T_1$ ,  $T_2$ ,  $T_3$  corresponded to the duration (sec) of the selected sucking bursts for each time period and  $B_1$ ,  $B_2$ ,  $B_3$  the average of a particular measure at each period. Sucking bursts were delineated by periods of pauses  $\geq 1.5$  sec.

## Statistics

Paired and independent *t*-test were used to compare variables between 1–2 and 6–8 oral feedings/day within group and between gestational groups, respectively. To identify the contribution of components demonstrating any change over time towards the observed increase in rate of milk intake, the difference of the variables measured showing any significant change between 1–2 and 6–8 oral feedings/day was entered into a multiple regression analysis. To determine whether the percentage occurrence of Sw-R interfacings was a random event at each time point, the Friedman test was utilized. Upon significance, the Wilcoxon signed rank test was used to test for significance between Sw-R interfacings at each time point.

## RESULTS

Table S2 shows infants' characteristics. When stratified by GAs (26/27 vs. 28/29 weeks), infants differed only by GA, birth weight and postnatal age at hospital discharge. No differences were observed between gestational groups in the number of days from start to full oral feeding and PMA when oral feeding was monitored at 1–2 and 6–8 oral feedings/day, as well as hospital discharge (Table S2). As outcomes were also similar between gestational groups (data not shown), they were combined for subsequent analyses. Rate of milk intake was significantly less at 1–2 than 6–8 oral feedings/day ( $1.9 \pm 1.0$  vs.  $4.3 \pm 1.8$  ml/min, respectively,  $p < 0.001$ ). Percent milk loss decreased over the same time period ( $22 \pm 14$  vs.  $10 \pm 7\%$ , respectively,  $p = 0.011$ ). Table S3 shows that only Sk stage, Sk rate, S amplitude and S slope increased over time. Sk rate was significantly greater than S rate at both periods. No changes were observed in Sw and Sk-Sw outcomes (Table S3). Of the factors that showed changes over time, the increase in rate of milk intake was significantly correlated only with changes occurring with Sk stage, S amplitude and slope ( $p \leq 0.023$ ,  $R^2 = 88.2\%$ ).

Infants born at 26/27-week GA exhibited greater COV than their 28/29-week GA counterparts for the time intervals S-E, t1, t2 and E-Sw at 1–2 oral feedings per day ( $p \leq 0.05$ ), and for time interval S-E, S amplitude and S-Sw at 6–8 oral feedings per day ( $p \leq 0.020$ ). This was observed in spite of the fact that both groups of infants were at similar PMA at these two time periods, i.e. 34 and 38 weeks, respectively. As infants born at 28/29-week GA advanced in oral feeding, COV in time interval between peak S and E (S-E) decreased ( $p = 0.008$ ). This was not observed in their younger preterm counterparts.

From the Sw-R interfacings results (Table S4), swallowing was favoured during DA and inhalation at 1–2 oral feedings/day and remained predominant during DA at 6–8 oral feedings/day.

## DISCUSSION

Caretakers of preterm infants are all too familiar with the issues their young patients have transitioning from tube to oral feeding. Immature sucking, uncoordinated suck-swallow-respiration are some of the reasons routinely given for such difficulty. Insofar as physiological functions mature at different times (5,23–25), we speculated that components implicated within specific functions, such as sucking, swallowing, also develop at different times and/or rates. Coordination of suck-swallow-respiration has been defined primarily as attained with a consistent ratio of 1:1:1 or 2:2:1 (21,26). Over the last few years, we have focused rather on a different concept of coordination, one that incorporates safety. While rhythmicity remains essential, swallowing needs to occur at a phase of the respiratory cycle, i.e. Sw-R interfacing, that minimizes the risk for aspiration (23).

With the above in mind, our aim was to identify components within these individual functions that would be maturing as clinically stable preterm infants transitioned to oral feeding. We



confirmed our first hypothesis that the developmental processes of oral feeding skills mature at different times and/or rates. Our second hypothesis was partially confirmed as GA appeared to have a greater impact than PMA on oral feeding skills during the time period this study was conducted. As the outcomes measured resulted from the integrative responses exhibited by the different musculatures implicated, they were used as indirect markers for the synchronization of muscles within a set of musculature (one function) or for the coordination between different sets of musculature (several functions). By measuring these outcomes between 1–2 and 6–8 oral feedings/day, it was possible to identify those demonstrating a steady level of maturity (no change) versus those that were maturing (increase/decrease). It is important to recognize that, during the time they were monitored, skills that remained unchanged may be already mature or have not yet begun to mature, while those that changed were maturing, but had not necessarily completed their maturation. To differentiate between these gradations, comparison of the infants' performance at 6–8 oral feedings/day with that of full-term infants during their first week of life (used as gold standard) would be necessary (23).

For the first hypothesis, our results allow for novel observations: 1. *Rate of milk intake* advanced as expected, but appeared to be primarily dependent upon improved Sk stage, strength and activation speed of the S musculature. This occurred in spite of improved synchronization of the perioral and Sk musculatures that led to a decreased milk leakage and increased Sk rate, respectively. However, this outcome has not yet fully matured based on our earlier observations that full-term infants at 1 week of life averaged  $7.1 \pm 1.3$  mL/min (23). 2. *Maturation of sucking* was characterized by improved Sk stage and rate, but not by increased use of S as the S/E ratio remained  $< 1$ . Infants still relied on the use of the immature sucking pattern consisting of E only. The time interval between peak S and E (S-E) remained unchanged suggesting that the coordination of the two musculatures was at the same level of synchrony when infants were taking 1–2 and 6–8 oral feedings/day. Although Sk stage has not yet reached that of 1-week-old full-term infants, i.e. stage 5 (5) with consistent rhythmic alternation of S and E, Sk rate attained  $\sim 1$  cycle/second, a characteristic of full-term infants (27). 3. *Maturation of suction* was reflected primarily by an increase in S amplitude and slope. S amplitude, as for Sk stage, has not yet completed its full maturation as we observed in an earlier study that 1-week-old full-term infants averaged  $-130 \pm 34.1$  mm Hg (23). S slope was defined as a reflection of the degree of synchronization of the muscles implicated in generating S; the greater the value, the faster their response or activation speed. Although, it would be expected for such synchrony to be a function of the bottle nipple physical characteristics, e.g. softness, nipple hole size, this may not be necessarily valid. Indeed, infants can modify their sucking skills so as to maintain a rate of milk transfer compatible with their level of Sk-Sw-R coordination (5,20,28,29). In a study comparing the rate of milk transfer of very low birth-weight infants, using three different bottle nipples within 24 h, we noted that infants demonstrated similar rate of milk transfer, but their sucking stage, suction amplitude and duration of the generated suction ( $t_1$ ) were significantly different between nipples at 1–2, but not 6–8 oral feedings/day (28). Based on this information, we speculate that the increase in S slope over time observed herein resulted more likely from an improved synchronization of the S musculature than a secondary effect due to the use of different bottle nipples. The S rate of  $< 1$  is readily explained by the observation that the use of the rhythmic alternation of S and E was inconsistent as the S/E ratio was  $< 1$ . Two plausible causes may be implicated: the generation of S has not fully developed and/or infants switched to using only E as it allows for a slower flow in order to maintain a rate of transfer compatible with their level of Sk-Sw-R coordination. 4. *Maturation of swallow and suck-swallow* appeared mature when the infants were initiated to oral feeding as they already were at the mature rate of 1/s and a ratio of 1:1, respectively (21,23,27). Also, no change over time was observed in the synchronization within the coordination of sucking (S and E) and swallowing musculature, i.e. Sw rate, Sk/Sw ratio, time interval between S-Sw and E-Sw. It is of interest to note that, within a sucking burst, very rarely did swallows occur between S and E. They occurred, rather, after E or before S. Although such observation is suggestive of a S-

E temporal sequence within a suck cycle, our study design and methodology do not allow for such conclusion. Studies specifically designed to address this question would help clarify this issue. For instance, the use of a combination of pressure recording of S and E along with advanced 3-D sonographic imaging technologies could identify the functional significance of jaw and lingual mechanics (9). 5. *Maturation of swallow-respiration* is not yet mature at 6–8 oral feedings/day as infants still swallowed during DA, a riskier phase of respiration. This confirms the observations made by other investigators as well as ourselves (23,25,30).

For our second hypothesis pertaining to oral feeding skills being dependent upon GA and/or PMA, the following observations are presented. GA dependency is verified by the differences in COV measured in our subjects when they were stratified between 26/27- and 28/29-week GA. Although ‘on the surface’, no significant differences were observed between groups for any of the outcomes measured, the additional COV analysis provided a discrete indication of immaturity, i.e. the infants born more prematurely did not reach the same levels of stability for certain skills as their older counterparts. This was more evident at the introduction than attainment of independent oral feeding; more specifically, at 1–2 oral feedings/day with the coordination of the S and E musculatures (S-E), synchronization of the S musculature (t1, t2) and coordination of E-Sw. By 6–8 oral feedings/day, synchronization of the S musculature appeared to have caught up with that of the 28/29-week gestation infants, but the functional stability of S amplitude and coordination of S and E and S-Sw musculatures still lagged. The greater variance in S-Sw may ensue from the instability observed between the coordination of S and E musculatures. There was also a significant decrease in the COV of S amplitude within the 28/29-week GA group over time. We interpret these results as evidence that the musculature implicated in generating S amplitude was better developed in the 28/29- than 26/27-week GA infants at the start of oral feeding and had continued to mature until they reach independent oral feeding, whereas such temporal maturation did not yet occur in the 26/27-week GA infants. Because both groups of infants were introduced and attained independent oral feeding at similar PMA, i.e. around 34 and 38 weeks, respectively, these observations lend support to our hypothesis that GA influences the *ex utero* development of oral feeding skills.

Preterm infants’ catch-up growth is a continual concern of physicians. As the primary frame of reference for such catchup is based on the intrauterine growth curve constructed from a small number of reference foetuses as standards, *ex utero* maturation is equated with *in utero* maturation (31). However, an increasing number of studies are showing that this is not equitable. Indeed, preterm infant after birth are in completely different environment, routinely subjected to aversive but necessary procedures, and receiving totally different nutrition (32, 33). The lack of PMA influence on oral feeding performance in our subjects may result from the fact that maturation of oral feeding skills is also influenced by exposure/practice. As our subjects were introduced to oral feeding around 33–34 weeks PMA, both groups of infants received comparable number of oral feeding experiences as they weaned from tube feeding. The notion that experience or ‘training’ enhances sucking skills is supported by our studies conducted in a similar preterm population whereby non-nutritive oral stimulation, offered prior to the introduction of oral feeding, accelerated attainment of independent oral feeding and specifically enhanced E amplitude (34,35).

In summary, our observations confirm that components of sucking, swallowing, respiration, along with their coordination mature at different times and rates when clinically stable 26- to 29-week GA infants were introduced to oral feeding. Some were in the process of maturing while others were already mature. Overall, this development was by no means complete when infants attained independent oral feeding with GA playing an influential role. A better understanding of the maturational processes would lead to more precise diagnoses of the causes of oral feeding difficulties and to greater insight into the limitations encountered by preterm infants when they transition to oral feeding. It is also expected that such knowledge will lead

to the development of preventive and therapeutic interventions that will facilitate their transition from tube to oral feeding.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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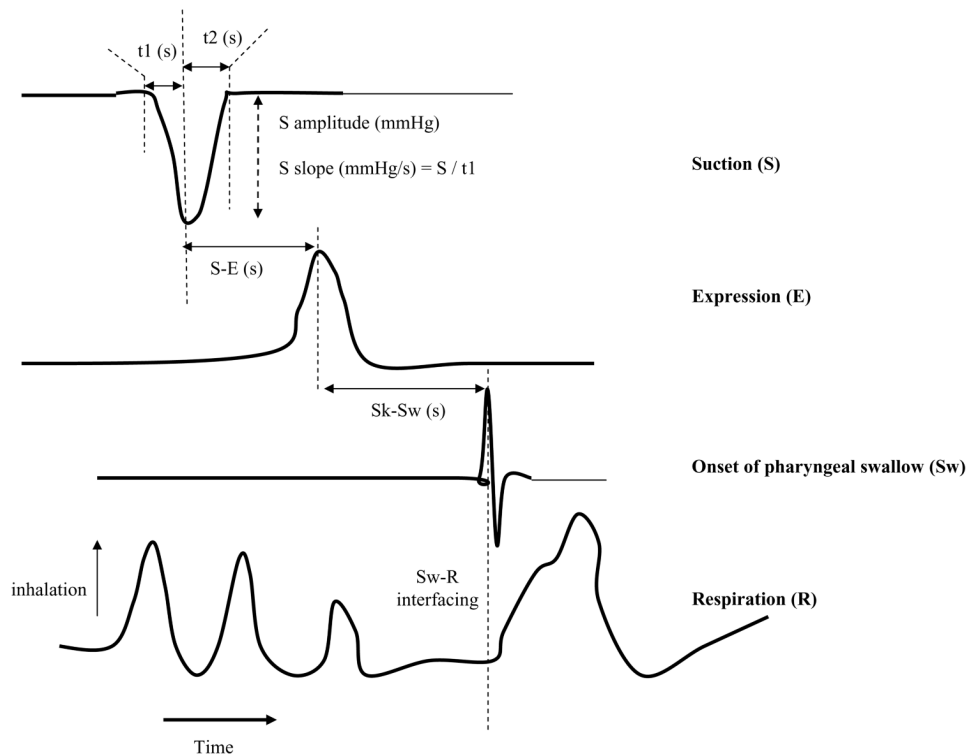
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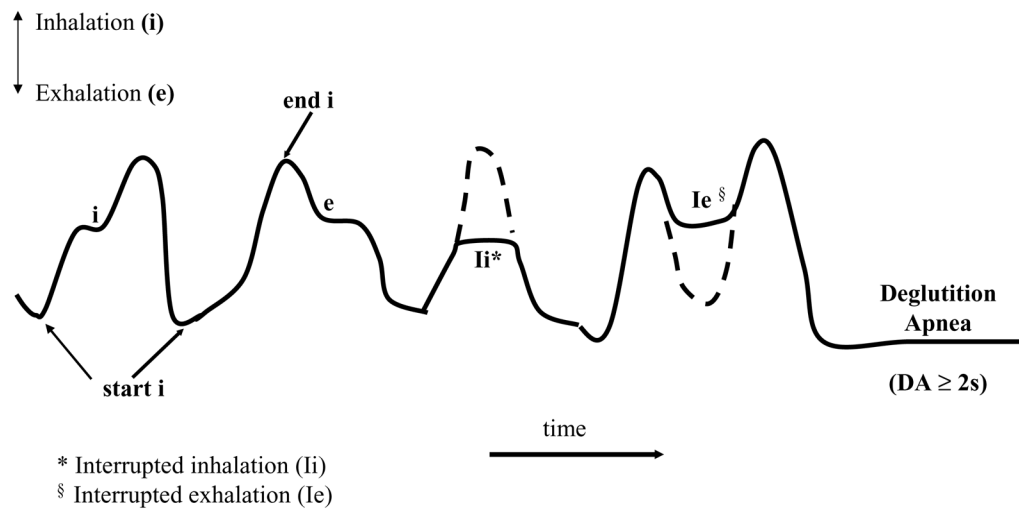
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**Figure 1.**

Schematic representing the simultaneous pressure recordings of sucking (suction and expression components), onset of swallowing and respiration (upward deflection: inhalation) over time. Dotted lines on each tracing delineate measures of time interval (sec). Swallow–respiration interfacing were identified by the time at which onset of pharyngeal swallowing and a particular respiratory phase occurred. The example shown by the dotted line between swallow and respiration is that of a swallow occurring at the beginning of inhalation.

## Swallow-Respiration Interfacing (Sw-R)



**Figure 2.**

Schematic describing the various swallow–respiration interfacing. Swallowing can occur during inhalation (i), end of inhalation/start of exhalation (end i), during exhalation (e), interrupting inhalation (ii), interrupting exhalation (ie) or during deglutition apnea defined as apnea  $\geq 2$  sec.